Claims as Pending

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This listing of the claims will replace all prior versions, and listings, of claims in the application.

- 1.-33. (Cancelled)
- 34. (Currently Amended) A method for treating a subject having, or at risk of having, a disorder which can be treated by increased <u>cerebral or coronary</u> vasodilation or inhibition of <u>cerebral or coronary</u> vasoconstriction, comprising:

administering to a subject in need of such treatment an agent that down-regulates S1P-binding EDG receptor signaling in an amount effective to treat the disorder.

wherein EDG receptor signaling is EDG-3 or EDG-5 receptor signaling and wherein the agent is an EDG receptor inhibitor.

- 35.-42. (Cancelled)
- 43. (Currently Amended) A method for increasing <u>cerebral or coronary</u> arterial blood flow in a subject who would benefit from increased <u>cerebral or coronary</u> arterial blood flow, comprising:

administering to a subject in need of such treatment an agent that down-regulates S1P-binding EDG receptor signaling in an amount effective to increase cerebral or coronary arterial blood flow,

wherein EDG receptor signaling is EDG-3 or EDG-5 receptor signaling and wherein the agent is an EDG receptor inhibitor.

- 44.-55. (Cancelled)
- 56. (Currently Amended) A method for inhibiting <u>cerebral or coronary</u> vasoconstriction in a subject who would benefit from inhibited <u>cerebral or coronary</u> vasoconstriction, comprising: administering to a subject in need of such treatment an agent that down-regulates S1P-

binding EDG receptor signaling in an amount effective to inhibit cerebral or coronary vasoconstriction.

wherein EDG receptor signaling is EDG-3 or EDG-5 receptor signaling and wherein the agent is an EDG receptor inhibitor.

- 57.-87. (Cancelled)
- 88. (Currently Amended) The method of claim 34, wherein the agent is an S1P-binding EDG-3 or EDG-5 receptor inhibitor.
- 89. (Withdrawn) The method of claim 88, wherein the S1P-binding EDG receptor inhibitor is selected from the group consisting of EDG-1 receptor inhibitor, EDG-3 receptor inhibitor, agent is an EDG-5 receptor inhibitor, and EDG-8 receptor inhibitor.
- 90. (Currently Amended) The method of claim 88, wherein the S1P-binding EDG receptor inhibitor agent is an EDG-3 receptor inhibitor.
- 91. (Currently Amended) The method of claim 88, wherein the S1P-binding EDG receptor inhibitor agent is sphingosine or suramin.
 - 92. (Cancelled)
- 93. (Currently Amended) The method of claim 34, wherein the disorder is selected from the group consisting of stroke, subarachnoid hemorrhage, granulomatous arteritis, transient ischemia attacks and cerebral vasospasm.
 - 94.-95. (Cancelled)
- 96. (Currently Amended) The method of claim 43, wherein the agent is an S1P-binding EDG-3 or EDG-5 receptor inhibitor.
- 97. (Withdrawn) The method of claim 96, wherein the S1P-binding EDG receptor inhibitor is selected from the group consisting of EDG-1 receptor inhibitor, EDG-3 receptor inhibitor, agent is an EDG-5 receptor inhibitor and EDG-8 receptor inhibitor.

- 98. (Currently Amended) The method of claim 96, wherein the S1P-binding EDG receptor inhibitor agent is an EDG-3 receptor inhibitor.
- 99. (Currently Amended) The method of claim 96, wherein the S1P-binding EDG receptor inhibitor agent is sphingosine or suramin.

100. (Cancelled)

- 101. (Currently Amended) The method of claim 43, wherein the subject is having, or is at risk of having, a stroke, a subarachnoid hemorrhage, granulomatous arteritis, transient ischemia attacks or a cerebral vasospasm.
- 102. (Currently Amended) The method of claim 43, wherein the <u>cerebral or coronary</u> arterial blood flow is cerebral artery blood flow.
- 103. (Currently Amended) The method of claim 43, further comprising co-administering a second agent to the subject with a condition treatable by the second agent in an amount effective to treat the condition, whereby the delivery of the second agent to a tissue of the subject is enhanced as a result of the increased <u>cerebral or coronary</u> arterial blood flow.
- 104. (Previously Presented) The method of claim 103, wherein the second agent is selected from the group consisting of analeptic, analgesic, anesthetic, adrenergic agent, anti-adrenergic agent, amino acids, antagonists, antidote, anti-anxiety agent, anti-cholinergic, anti-convulsant, anti-depressant, anti-emetic, anti-epileptic, anti-hypertensive, anti-fibrinolytic, anti-hyperlipidemia, anti-migraine, anti-nauseant, anti-neoplastic (brain cancer), anti-obsessional agent, anti-obesity agent, anti-parkinsonian, anti-psychotic, appetite suppressant, blood glucose regulator, cognition adjuvant, cognition enhancer, dopaminergic agent, emetic, free oxygen radical scavenger, glucocorticoid, hypocholesterolemic, hypolipidemic, histamine H2 receptor antagonists, immunosuppressant, inhibitor, memory adjuvant, mental performance enhancer, mood regulator, mydriatic, neuromuscular blocking agent, neuroprotective, NMDA antagonist, post-stroke and post-head trauma treatment, psychotropic, sedative,

sedative-hypnotic, serotonin inhibitor, tranquilizer, and treatment of cerebral ischemia, calcium channel blockers, free radical scavengers - antioxidants, GABA agonists, glutamate antagonists, AMPA antagonists, kainate antagonists, competitive and non-competitive NMDA antagonists, growth factors, opioid antagonists, phosphatidylcholine precursors, serotonin agonists, sodium-and calcium-channel blockers, and potassium channel openers.

105. (Previously Presented) The method of claim 103, wherein the second agent is tissue plasminogen activator (TPA).

106.-107. (Cancelled)

- 108. (Currently Amended) The method of claim 56, wherein the agent is an S1P binding EDG-3 or EDG-5 receptor inhibitor.
- 109. (Withdrawn) The method of claim 108, wherein the S1P-binding EDG-receptor inhibitor is selected from the group consisting of EDG-1 receptor inhibitor, EDG-3 receptor inhibitor, agent is an EDG-5 receptor inhibitor and EDG-8 receptor inhibitor.
- 110. (Currently Amended) The method of claim 108, wherein the S1P-binding EDG receptor inhibitor agent is an EDG-3 receptor inhibitor.
- 111. (Currently Amended) The method of claim 108, wherein the S1P binding EDG receptor inhibitor agent is sphingosine or suramin.

112. (Cancelled)

- 113. (Currently Amended) The method of claim 56, wherein the subject is having or is at risk of having a stroke, a subarachnoid hemorrhage, granulomatous arteritis, transient ischemia attacks or a cerebral vasospasm.
- 114. (Currently Amended) The method of claim 56, wherein the <u>cerebral or coronary</u> vasoconstriction is cerebral vasoconstriction.

115.-120. (Cancelled)

- 121. (Currently Amended) The method of claim 34, wherein the increased <u>cerebral or coronary</u> vasodilation or inhibition of <u>cerebral or coronary</u> vasoconstriction is needed in a cerebral artery.
- 122. (Previously Presented) The method of claim 121, wherein the cerebral artery is selected from the group consisting of basilar artery, internal carotid artery, external carotid artery, anterior cerebral artery, middle cerebral artery, posterior cerebral artery, vertebral artery, posterior inferior cerebellar artery and middle meningeal artery.
- 123. (Previously Presented) The method of claim 121, wherein the cerebral artery is a basilar artery or middle cerebral artery.
- 124. (Currently Amended) The method of claim 34, wherein the increased <u>cerebral or coronary</u> vasodilation or inhibition of <u>cerebral or coronary</u> vasoconstriction is needed in a coronary artery.
- 125. (Previously Presented) The method of claim 102, wherein the cerebral artery blood flow is in a cerebral artery selected from the group consisting of basilar artery, internal carotid artery, external carotid artery, anterior cerebral artery, middle cerebral artery, posterior cerebral artery, vertebral artery, posterior inferior cerebellar artery and middle meningeal artery.
- 126. (Previously Presented) The method of claim 102, wherein the cerebral artery blood flow is basilar artery or middle cerebral artery blood flow.
- 127. (Currently Amended) The method of claim 43, wherein the <u>cerebral or coronary</u> arterial blood flow is coronary artery blood flow.
- 128. (Previously Presented) The method of claim 114, wherein the cerebral vasoconstriction is in a cerebral artery selected from the group consisting of basilar artery,

internal carotid artery, external carotid artery, anterior cerebral artery, middle cerebral artery, posterior cerebral artery and middle meningeal artery.

- 129. (Previously Presented) The method of claim 114, wherein the cerebral vasoconstriction is basilar artery or middle cerebral vasoconstriction.
- 130. (Currently Amended) The method of claim 56, wherein the <u>cerebral or coronary</u> vasoconstriction is coronary artery vasoconstriction.
- 131. (Currently Amended) The method of claim 34, wherein the S1P-binding EDG receptor signaling is EDG-3 receptor signaling.
- 132. (Withdrawn) The method of claim 34, wherein the S1P-binding EDG receptor signaling is EDG-5 receptor signaling.
 - 133. (Cancelled)
- 134. (Currently Amended) The method of claim 43, wherein the S1P-binding EDG receptor signaling is EDG-3 receptor signaling.
- 135. (Withdrawn) The method of claim 43, wherein the S1P binding EDG receptor signaling is EDG-5 receptor signaling.
 - 136. (Cancelled)
- 137. (Currently Amended) The method of claim 56, wherein the S1P-binding EDG receptor signaling is EDG-3 receptor signaling.
- 138. (Withdrawn) The method of claim 56, wherein the S1P-binding EDG receptor signaling is EDG-5 receptor signaling.

139. (Cancelled)

140. (New) A method for treating a subject having, or at risk of having, a disorder which can be treated by increased cerebral vasodilation or inhibition of cerebral vasoconstriction, comprising

downregulating EDG-3 receptor signaling in a subject in need thereof to an extent effective to treat the disorder.

- 141. (New) The method of claim 140, wherein the disorder is selected from the group consisting of stroke, subarachnoid hemorrhage, granulomatous arteritis, transient ischemia attacks and cerebral vasospasm.
- 142. (New) The method of claim 140, wherein the cerebral arterial blood flow is basilar artery or middle cerebral arterial blood flow.
- 143. (New) A method for increasing cerebral arterial blood flow in a subject who would benefit from increased cerebral arterial blood flow, comprising

downregulating EDG-3 receptor signaling in a subject in need thereof to an extent effective to increase cerebral arterial blood flow.

- 144. (New) The method of claim 143, wherein the cerebral arterial blood flow is basilar artery or middle cerebral arterial blood flow.
- 145. (New) The method of claim 143, wherein the subject is having or is at risk of having a stroke, a subarachnoid hemorrhage, granulomatous arteritis, transient ischemia attacks or a cerebral vasospasm.
- 146. (New) A method for inhibiting cerebral or coronary vasoconstriction in a subject who would benefit from inhibited cerebral vasoconstriction, comprising

downregulating EDG-3 receptor signaling in a subject in need thereof to an extent effective to inhibit cerebral vasoconstriction.

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147. (New) The method of claim 146, wherein the cerebral vasoconstriction is basilar artery or middle cerebral vasoconstriction.

148. (New) The method of claim 146, wherein the subject is having or is at risk of having a stroke, a subarachnoid hemorrhage, granulomatous arteritis, transient ischemia attacks or a cerebral vasospasm.